VIRTUAL STAINING OF CELLS IN DIGITAL HOLOGRAPHIC MICROSCOPY IMAGES USING GENERAL ADVERSARIAL NETWORKS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Ser. No. 62/560,272 filed Sep. 19, 2017, which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

[0002] The present invention relates generally to virtual staining of cells, and, more particularly, to virtual staining of cells in digital holographic microscopy images using general adversarial networks with cycle consistency.

BACKGROUND

[0003] Digital holographic microscopy (DHM), also known as interference phase microscopy, is an imaging technology that provides the ability to quantitatively track sub-nanometric optical thickness changes in transparent specimens. Unlike traditional digital microscopy, in which only intensity (amplitude) information about a specimen is captured, DHM captures both phase and intensity. The phase information, captured as a hologram, can be used to reconstruct extended morphological information (such as depth and surface characteristics) about the specimen using a computer algorithm. Modern DHM implementations offer several additional benefits, such as fast scanning/data acquisition speed, low noise, high resolution and the potential for label-free sample acquisition

[0004] Off-axis DHM systems create holograms where there is a modulating sinusoidal fringe pattern over the entire field of view due to a small angle between the object and reference beams. In other words, plane waves impinging a sensor surface interfere destructively and constructively at the location of the sensor and thus form the sinusoidal pattern. Furthermore, as depicted in FIG. 1, a reference beam 20 is created from an object beam 10 using a pin hole at the location of the optical Fourier-plane (or conjugated plane to the Fourier-plane) to erase the object spatial signature and to provide a uniform plane waves for creating an interference or hologram image which may be stored and displayed to a user.

[0005] DHM is used in hematology to image different cells within a blood sample. When the beam passes through the cell to be imaged, it gets refracted based on the cell characteristics. These refraction variations can be captured through DHM as changes in the optical thickness within the nucleus. In white blood cells (WBCs), namely, basophils, eosinophils, lymphocytes, monocytes and neutrophils, the nuclei and the membranes have different properties and the structure of the cell constituents differ based on the cell type. Thus, the appearance of the DHM image changes depending on the cell type.

[0006] DHM images can thus be used to differentiate different types of WBCs within a blood sample. Cell type differentiation and counting of WBCs is an important aspect of a complete blood count (CBC) because, among other reasons, imbalance in certain proportions of the different cell types may indicate different autoimmune diseases and yield different patient diagnoses. Thus, a clinician can use captured DHM images of a blood sample in patient diagnosis.

[0007] Conventionally, counts of different WBC types may be obtained by providing a blood sample to an automated machine, such as a laser flow cytometer, which performs an automated count and analysis. In order to confirm or supplement the automated results, or in the absence of an automated machine, blood cells are also manually examined under a microscope and the different types of WBCs are counted and reviewed by a clinician. In order to be able to visually distinguish the different WBC types, the blood sample is stained with a dye before examination, such as through a peripheral blood smear. A blood film may be made by placing a drop of blood on one end of a glass slide and using a spreader to disperse the blood sample into a monolayer over the slide's length. The nucleus of each different type of WBC absorbs the stain differently, for example, as shown in FIG. 2, allowing the clinician to count and examine the different WBCs in a blood smear sample.

[0008] The manual blood staining process is time and labor consuming. Each sample must go through the blood smear process and the clinician must look at the sample under the microscope and look for and count the different cell types. This process is inefficient. DHM images have become an alternative to conventional microscopy and can be used to examine a blood sample and count the different types of WBCs in the sample. However, DHM images, such as those shown in the example DHM images of FIG. 3, may not include sufficient detail or resolution in order to allow each cell type to be easily identified and categorized by the clinician.

[0009] The present disclosure is directed to overcoming these and other problems of the prior art, such as through providing a cell visualization system that virtually generates stained images from DHM images, replacing or supplementing the need to perform the manual staining process. Moreover, the present disclosure is directed to overcoming a problem of DHM imaging which renders it difficult to train an automated system in determining how to identify and present each virtually-stained cell. In particular, since it is infeasible to obtain the stained image and the corresponding DHM image for the same cell because of the nature of each process, the virtual stain cannot simply be a reproduction of an actual stain. The present disclosure is additionally directed to overcoming this problem associated with training the cell visualization system.

SUMMARY

[0010] In one aspect, embodiments of the present disclosure are directed to a computer-implemented method for producing a virtually stained digital holographic microscopy (DHM) image. The method includes acquiring an image conversion algorithm which was trained using generative adversarial networks and receiving a DHM image acquired using a DHM device, the DHM image including depictions of one or more cells. The method further includes virtually staining the DHM image by processing the DHM image using the image conversion algorithm. The virtually stained DHM image includes digital colorization of the one or more cells to imitate the appearance of a corresponding actually stained cell.

[0011] In another aspect, embodiments of the present disclosure are directed to another computer-implemented